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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/234,182	01/20/1999	VANESSA HSEI	P1085R4-1A	6433
25213	7590	02/03/2004	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP 275 MIDDLEFIELD ROAD MENLO PARK, CA 94025-3506			ROARK, JESSICA H	
			ART UNIT	PAPER NUMBER

1644

DATE MAILED: 02/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/234,182

Applicant(s)

HSEI ET AL.

Examiner

Jessica H. Roark

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 19-22, 26-29 and 31-36 is/are pending in the application.
- 4a) Of the above claim(s) 2-4, 6, 7, 20, 22 and 27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 5, 19, 21, 26, 28, 29 and 31-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 January 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Petition Decision - Approved*.

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### RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/12/03 has been entered.

2. Applicant's amendment, filed 11/12/03, is acknowledged.  
Claims 8-18, 23-25 and 30 have been cancelled previously.  
Claims 1-7, 19-22, 26-29 and 31-36 are pending.

Claims 2-4, 6-7, 20, 22 and 27 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention, election having been confirmed without traverse in Paper No. 15.

*Claims 1, 5, 19, 21, 26, 28-29 and 31-36 are under consideration in the instant application.*

3. This Office Action will be in response to applicant's arguments, filed 11/12/03.  
The rejections of record can be found in the previous Office Action.

### ***Drawings***

4. Applicant's petition filed under 37 CFR 1.84(a)(2) has been approved. Please see the attached Paper.  
5. As previously noted, the drawings filed 1/22/03 have been approved by the Draftsman.

### ***Claim Rejections - 35 USC § 112 first paragraph***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

7. Claims 1, 5, 19, 21, 26, 28-29 and 31-36 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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Applicant's arguments, filed 11/12/03, have been fully considered but have not been found convincing for the reasons of record.

In response to the rejection of record Applicant argues that the specification provides sufficient guidance as to how to select the desired conjugates in which only a single Cys is derivatized with PEG. Applicant points to pages 77-79 and pages 221-226.

The Examiner yet again acknowledges that several conjugates of antibodies and antibody fragments to PEG are disclosed in the specification (e.g., the conjugation of a single PEG to the free thiol of the unpaired cysteine at the COOH terminus of the Fab' fragment, as disclosed on pages 216-220 of the specification). However, at issue is whether the specification provides sufficient guidance with respect to the particular conjugate recited in the instant claims, which requires that a single PEG be attached to one of the interchain Cys of an Fab' molecule that has not only the interchain Cys available for PEGylation, but also the Cys at the COOH terminus of the molecule.

The guidance in the specification pointed to by Applicant on page 221-226 address PEGylation of a different molecule (an F(ab')<sub>2</sub>) and uses a coupling chemistry that derivatizes Lys, not Cys.

The Examiner acknowledges that the specification does provide guidance as to how to select derivatives in which only a single PEG has been added (pages 77-79); however, there still does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan could make the instantly recited molecule which requires not only a single PEG, but also a single PEG in a particular location (the interchain Cys versus the COOH Cys).

For the reasons of record the Examiner therefore maintains that it would require undue experimentation of the skilled artisan to determine how to covalently couple a *single* PEG to an Fab' fragment in which one of the cysteines which ordinarily forms a disulfide bridge with another cysteine present in the opposite chain (i.e., using a cysteine ordinarily part of the heavy-light interchain disulfide bridge) as required by the claim language to be covalently coupled when insufficient guidance is provided as to avoid coupling of the second free cysteine present at the carboxy terminus of the Fab' fragment.

The rejection is therefore maintained.

Applicant is invited to provide evidentiary support that the specification is enabling as filed for the production of a conjugate having the recited properties.

### ***Double Patenting***

8. Claims 1, 5, 19, 21, 31-35 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, 13, 15-16, 18, 19, 21, 24, 26, 29, 32-37 of copending Application No. USSN 09/489,394. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '394 application recite all the limitations recited in the instant claims, indicating that the limitations set forth in the instant claims were obvious embodiments of the invention claimed in USSN 09/489,394.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments, filed 11/12/03, have been fully considered. However, co-pending application USSN 09/489,394 still was not available to the Examiner for review.

It is acknowledged that Applicant's Remarks indicate a copy of the current co-pending claims was provided as an attachment to Applicant's Response of 11/12/03. However, the attachment was not found as part of the instant file.

*Applicant is invited to contact the Examiner regarding submission of a courtesy copy of the co-pending claims so that this issue may be resolved.*

However, until such time as it is established that the claims are patentably distinct, the rejection is maintained.

### ***Conclusion***

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (571) 272-0848. The examiner can normally be reached Monday from 8:30 to 5:00, and Tuesday/Thursday from 10:00 to 4:00. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (571) 272-0841. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number for before Final submissions is (703) 872-9306.

Jessica Roark, Ph.D.  
Patent Examiner  
Technology Center 1600  
January 29, 2004

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PHILLIP GAMBEL, PH.D  
PRIMARY EXAMINER  
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1/29/04